

THAT WHICH IS CLAIMED IS:

1. A method for preparing an injectable formulation of interferon-beta (IFN- β) comprising:
 - a) preparing a first solution comprising IFN- β , isolating a pool of purified IFN- β from this solution, and precipitating said IFN- β from this pool using an alcohol to form a precipitate;
 - b) dissolving said precipitate in guanidine hydrochloride (HCl) to form a second solution comprising resolubilized denatured IFN- β and guanidine HCl;
 - c) diluting said second solution into a first buffer to obtain a third solution comprising resolubilized renatured IFN-beta and residual guanidine HCl; and
 - d) removing residual guanidine HCl from said third solution by diafiltration or dialysis of said third solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN- β is prepared.
2. The method of claim 1, wherein said second buffer contains arginine or sodium chloride.
3. The method of claim 1, wherein said first buffer has a pH of about 5.0 to about 8.0, and wherein said residual guanidine HCl is present in said third solution at a concentration of 1.6 M or less.
4. The method of claim 1, wherein said IFN- β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.
5. The method of claim 1, wherein said IFN- β is glycosylated or unglycosylated.
6. The method of claim 1, wherein said IFN- β is recombinantly produced.

7. The method of claim 1, wherein said IFN- β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

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8. A method for preparing an injectable formulation of interferon-beta (IFN- β), said method comprising denaturation of IFN- β with guanidine hydrochloride (HCl) followed by renaturation of the IFN- β via dilution into a first buffer to obtain a renatured IFN- β solution comprising residual guanidine HCl, and removing said residual guanidine HCl from said renatured IFN- β solution by diafiltration or dialysis of said renatured IFN- β solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN- β is prepared.

9. The method of claim 8, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said renatured IFN- β solution at a concentration of 1.6 M or less.

10. The method of claim 9, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said renatured IFN- β solution at a concentration of 0.2 M or less.

11. The method of claim 10, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said renatured IFN- β solution at a concentration of 0.1 M or less.

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12. The method of claim 8, wherein said IFN- β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

13. The method of claim 8, wherein said IFN- β is glycosylated or unglycosylated.

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14. The method of claim 8, wherein said IFN- β is recombinantly produced.

15. The method of claim 8, wherein said IFN- β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated
5 using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

16. A method for preparing a composition comprising substantially monomeric interferon-beta (IFN- β), said method comprising:
10 a) preparing a precipitate of substantially purified IFN- β ;
b) dissolving said precipitate in guanidine hydrochloride (HCl) to obtain a first solution comprising resolubilized denatured IFN- β ; and
c) renaturing said IFN- β by dilution of said first solution with a buffer solution.

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17. The method of claim 16, wherein said buffer solution has a pH of about 5.0 to about 8.0.

18. The method of claim 16, wherein said IFN- β has the amino acid sequence
20 set forth in SEQ ID NO:1 or SEQ ID NO:2.

19. The method of claim 16, wherein said IFN- β is glycosylated or unglycosylated.

20. The method of claim 16, wherein said IFN- β is recombinantly produced.
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21. The method of claim 16, wherein said IFN- β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of
30 12, and a gap penalty of 4.

22. A method for preparing an injectable formulation of interferon-beta (IFN- β), said method comprising:

- a) obtaining a sample comprising substantially purified IFN- β ;
- b) mixing said sample with guanidine hydrochloride (HCl) to obtain a
- 5 first solution comprising solubilized denatured IFN- β ;
- c) diluting said first solution into a first buffer to obtain a second solution comprising solubilized renatured IFN-beta and residual guanidine HCl; and
- d) removing residual guanidine HCl from said second solution by
- 10 diafiltration or dialysis of said second solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN- β is prepared.

23. The method of claim 22, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 1.6 M or less.

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24. The method of claim 23, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 0.2 M or less.

20 25. The method of claim 24, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said renatured IFN- β solution at a concentration of 0.1 M or less.

26. The method of claim 22, wherein said IFN- β has the amino acid sequence

25 set forth in SEQ ID NO:1 or SEQ ID NO:2.

27. The method of claim 22, wherein said IFN- β is glycosylated or unglycosylated.

30 28. The method of claim 22, wherein said IFN- β is recombinantly produced.

29. The method of claim 22, wherein said IFN- β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

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30. A method for preparing a composition comprising substantially monomeric interferon-beta (IFN- β), said method comprising:

- a) preparing a sample comprising substantially purified IFN- β ;
- b) mixing said sample with guanidine hydrochloride (HCl) to obtain a
10 first solution comprising solubilized denatured IFN- β ; and
- c) renaturing said IFN- β by dilution of said first solution with a buffer
solution.

31. The method of claim 30, wherein said buffer solution has a pH of about
15 3.0 to about 5.0.

32. The method of claim 30, wherein said IFN- β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

20 33. The method of claim 30, wherein said IFN- β is glycosylated or unglycosylated.

34. The method of claim 30, wherein said IFN- β is recombinantly produced.

25 35. The method of claim 30, wherein said IFN- β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

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